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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/005,200 | 12/05/2001 | Michael R. Wessels | B00801/70237 (ERG/MXA) | 8283 |

7590 10/30/2003

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| EXAMINER | |
|---|---|
| FORD, VANESSA L | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1645 | 15 |

DATE MAILED: 10/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application N . | Applicant(s) | |
|---|---|---|---|
| | 10/005,200 | WESSELS ET AL. | |
| | Examiner | Art Unit | |
| | Vanessa L. Ford | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**P riod for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *91,115,139-141,143,145-147,151-153,155,157-159 and 161* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19,21-23,45 and 68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *See Continuation Sheet* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 December 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .



Continuation of Disposition of Claims: Claims pending in the application are 1-19,21-23,45,68,91,115,139-141,143,145-147,151-153, 155,157-159 and 161.

Continuation of Disposition of Claims: Claims subject to restriction and/or election requirement are 1-19,21-23,45,68,91,115,139-141,143,145-147,151-153, 155,157-159 and 161.

## DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 1-19, 21-23, 45 and 68 filed July 30, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 91,115, 139-141, 143, 145-147, 149, 151-153, 155, 157-159 and 161 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 1-19, 21-23, 45 and 68 recite the term "reduce the likelihood". It is unclear as to what the applicant is referring? Thus, the metes and bounds of "reduce the likelihood" cannot be ascertained. Clarification as to the meaning of this term is required.

### *Drawings*

3. The drawings are objected to by the Draftsman under 37 CFR 1.84 or 1.152. See the attached form PTO 948.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-19, 21-23, 45 and 68 are rejected under 35 U.S.C. unpatentable over Yutaka *(JP 6 107 550, published April 19, 1994).*

Claims 1-19, 21-23, 45 and 68 are drawn to a method of treating a subject to reduce the likelihood of streptococcal or staphylococcal infection comprising administering orally to a subject in need of such treatment an agent that binds to a hyaluronic acid-binding region of a CD44 protein in an amount effective to interfere with the adhesion of streptococcal bacteria to CD44 protein in the subject and inhibit streptococcal colonization of the pharynx wherein either one or both of the following conditions applies: the treatment is free of Echinacea or the agent is administered in a dose greater than 0.2 mg wherein the agent is hyaluronic acid or an analog of hyaluronic acid.

Yutaka teaches the use of hyaluronic acid for treatment of inflammation of the mucous membrane in amygdalitis, pharyngitis and larynxitis (streptococcal and staphylococcal infections)(see the Abstract). Yutaka teaches that hyaluronic acid can be bonded to the inflammation part of the mucous membrane from the oral cavity to the upper respiratory tract and cure inflammation by oral administration of hyaluronic acid.

Yutaka teaches a method of treating a subject to reduce the likelihood of streptococcal or staphylococcal infections wherein the treatment is free of Echinacea. Claim limitations such as dosage requirements, time periods and number of administrations are being viewed as limitations of optimizing experimental parameters".

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the hyaluronic acid as taught by Yutaka in the method of treating against streptococcal and staphylococcal infections because Yutaka teaches that hyaluronic acid can be bonded to the inflammation part of the mucous membrane from the oral cavity to the upper respiratory tract and cure inflammation, thereby preventing the adhesion of bacteria to the CD44 protein in the subject and inhibiting streptococcal colonization of the pharynx. It would be expected barring evidence to the contrary, that the hyaluronic acid as taught by Yutaka would be effective in a method of treating against streptococcal and staphylococcal infections because oral administration of hyaluronic acid cures inflammation of the be bonded to the inflammation part of the mucous membrane from the oral cavity to the upper respiratory tract.

5. Claims 1-19, 21-23, 45 and 68 are rejected under 35 U.S.C. 103(a) as unpatentable over Schrager et al *(J. Clin. Invest., Volume 98, Number 9, November 1996).*

Claims 1-19, 21-23, 45 and 68 are drawn to a method of treating a subject to reduce the likelihood of streptococcal or staphylococcal infection comprising

administering orally to a subject in need of such treatment an agent that binds to a hyaluronic acid-binding region of a CD44 protein in an amount effective to interfere with the adhesion of streptococcal bacteria to CD44 protein in the subject and inhibit streptococcal colonization of the pharynx wherein either one or both of the following conditions applies: the treatment is free of Echinacea or the agent is administered in a dose greater than 0.2 mg.

Schrager et al teach that the monoclonal antibody to CD44, IM7.8.1 blocked attachment not only to stains that produced measurable amounts of capsule but also to strains that produced very low amounts of capsule (page 1715, 1st column). Schrager et al teach a method of treating a subject to reduce the likelihood of streptococcal or staphylococcal infections wherein the treatment is free of Echinacea. Claim limitations such as dosage requirements, time periods and number of administrations are being viewed as limitations of optimizing experimental parameters".

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the IM7.8.1 antibody as taught by Schrager et al in the method of treating against streptococcal and staphylococcal infections because Schrager et al teach that the monoclonal antibody to CD44, IM7.8.1 blocked attachment not only stains that produced measurable amounts of capsule but also strains that produced very low amounts of capsule (page 1715, 1st column), thereby preventing the adhesion of bacteria to the CD44 protein in the subject and inhibiting bacterial colonization of the pharynx. It would be expected barring evidence to the contrary, that the IM7.8.1 antibody would be effective in a method of treating against streptococcal

and staphylococcal infections because the IM7.8.1 antibody prevents colonization of the pharynx .

6. Claims 1-19, 21-23, 45 and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zheng et al *(The Journal of Cell Biology, Volume 130, Number 2, July 1995).*

Claims 1-19, 21-23, 45 and 68 are drawn to a method of treating a subject to reduce the likelihood of streptococcal infection comprising administering orally to a subject in need of such treatment an agent that binds to a hyaluronic acid-binding region of a CD44 protein in an amount effective to interfere with the adhesion of streptococcal bacteria to CD44 protein in the subject and inhibit streptococcal colonization of the pharynx wherein either one or both of the following conditions applies: the treatment is free of Echinacea or the agent is administered in a dose greater than 0.2 mg.

Zheng et al teach antibodies that block hyaluronan (hyaluronic acid) recognition, these antibodies include KM114, KM81, KM201, RAMBM55.5 and D12) (page 493). Zheng et al suggest that there might be naturally occurring substances that modulate ligand recognition by CD44, the cell adhesion molecule. Zheng et al teach that their observations with enhancing and inhibiting antibodies indicate that such regulatory molecules could function through multiple sites and mechanisms. Zheng et al suggest that monoclonal antibodies to CD44, for example KM114 has a high affinity for CD44 than its ligand and blocks binding to the CD44 (page 493, 2$^{nd}$ column). Zheng et al

teach a method of treating a subject to reduce the likelihood of streptococcal or staphylococcal infections wherein the treatment is free of Echinacea. Claim limitations such as dosage requirements, time periods and number of administrations are being viewed as limitations of optimizing experimental parameters".

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the monoclonal antibodies of Zheng et al in the method of treating against streptococcal and staphylococcal infections because Zheng et al teach antibodies that block hyaluronan (hyaluronic acid) recognition. It would be expected barring evidence to the contrary, the monoclonal antibodies of Zheng et al would be effective in a method of treating against streptococcal and staphylococcal infections because Zheng et al suggest that monoclonal antibodies to CD44, for example KM114 has a high affinity for CD44 than its ligand and blocks binding to the CD44. It would be expected barring evidence to the contrary, that the monoclonal antibodies as taught by Zheng et al would be effective in a method of treating against streptococcal and staphylococcal infections because the monoclonal antibodies inhibit binding to CD44 thereby preventing colonization of the pharynx.

***Pertinent Prior Art***

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure Green et al *(Experimental Cell Research, 178(1988), 224-232)* and Schrager et al *(Abstracts of the IDSA 35th Annual Meeting, 1997).*

***Status of Claims***

8. No claims are allowed.

***Conclusion***

9. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
October 10, 2003

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